
Therapeutic applications of the PhiC31 integrase system.

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Public Summary:

This review article focuses on developments that have occurred in the phiC31 integrase system over the past several years. The article describes how this integrase system functions to insert genes into specific locations in the chromosomes. The mode of action of the system is described, and how it has been used for gene therapy studies is summarized. Studies using the integrase system in live animals and in isolated cells are reviewed. In particular, the use of the phiC31 integrase system as a tool for gene addition in stem cells is described and is relevant to the goals of CIRM. Studies are described that illustrate how the system has been used to date in various adult stem cells types. In addition, the use of integrase to create induced pluripotent stem cells from mouse and human cells is reviewed. This is an application of the integrase technology that is likely to be useful for development of cell therapy strategies.

Scientific Abstract:

The potential use of the PhiC31 integrase system in gene therapy opens up the possibilities of new treatments for old diseases. PhiC31 integrase mediates the integration of plasmid DNA into the chromosomes of mammalian cells in a sequence-specific manner, resulting in robust, long-term transgene expression. In this article, we review how PhiC31 integrase mediates transgene integration into the genomes of target cells and summarize the recent preclinical applications of the system to gene therapy. These applications encompass in vivo studies in liver and lung, as well as increasing ex vivo uses of the system, including in neural and muscle stem cells, in cord-lining epithelial cells, and for the production of induced pluripotent stem cells. The safety of the PhiC31 integrase system for gene therapy is evaluated, and its ability to provide treatments for hemophilia is discussed. We conclude that gene therapy strategies utilizing PhiC31 integrase offer great promise for the development of treatments in the future.

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